Antidepressant and anxiolytic medication use and mortality risk in people with dementia in Northern Ireland: a nested case-control study

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Introduction

Antidepressant and anxiolytic medications are frequently prescribed for the management of depression and anxiety in people with dementia (PwD)[1] and their use is more extensive in PwD compared to those without dementia.[2] Limited evidence exists to support the use of antidepressant and anxiolytic medications in PwD;[3] these medications may contribute to potentially inappropriate prescribing and be associated with mortality.[4] This study aimed to investigate trends in prescribing of these medications and the association between exposure to antidepressants and anxiolytics and mortality risk among PwD.

Methods

Design

- A nested case-control study was conducted using record linkage of five administrative population-based data sources in Northern Ireland (NHAIS, EPD, PAS, GRO, NINIS) between 2010 and 2020.
- The study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.[5]

Data access

- The Honest Broker Service (HBS) is the Trusted Research Environment for accessing healthcare-related service user data for analysis in NI. The HBS provides access to de-identified or aggregated data for approved health and social care-related research.

Selection of cases and controls

- Dementia cases (identified if a medication indicated for dementia management was prescribed from 2012 following a one-year washout period; Figure 1) were matched to one control (based on age and sex).

Exposures

- Exposure to antidepressant and anxiolytic medications was assessed from prescribing records two years prior to dementia diagnosis (indicated by date of first dispensing of dementia medication) until six months prior to death or end of study.

Analysis

- Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using conditional logistic regression after adjusting for demographic factors and comorbidities such as marital status, level of deprivation, urban/rural status and medications used for comorbidities.
- Sensitivity analyses were undertaken assessing the length of exposure period and number of prescriptions issued.

NHAIS: National Health application and Infrastructure Services; EPD: Enhanced Prescribing Database; PAS: Patient Administration System; GRO: General Register Office; NINIS: Northern Ireland Neighbourhood Information System

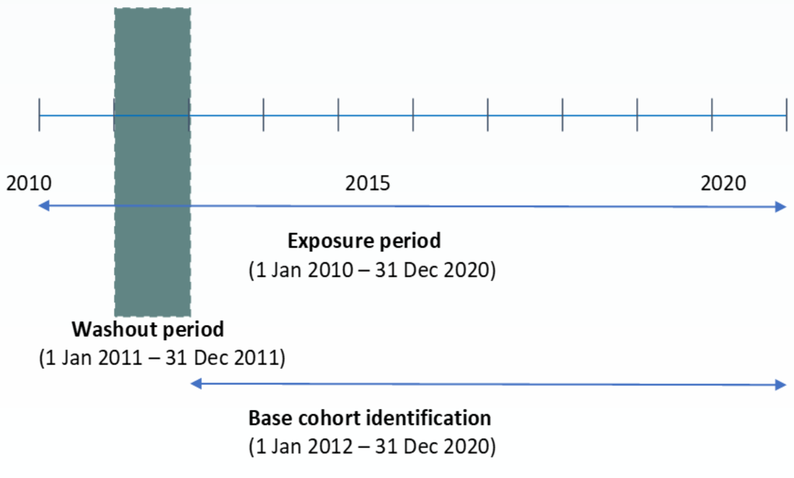

Figure 1: Identification of study population and timeline

Results

The study cohort comprised 31,525 PwD, of whom 16,302 died. After exclusions were applied, the cohort was converted to case-control data with 14,420 cases (i.e. those who died) and 14,361 controls (i.e. those who did not die) (Figure 2).

Figure 2: Identification of cases for case-control dataset
Individuals were excluded if they had a dementia diagnosis within two years of the end of study, if they died within two years of dementia diagnosis, or if the date of diagnosis or date of death were missing.

Prescribing trends

Anxiolytic medications were prescribed to almost half of cases **(*n*=6,484, 44.8%)** and over one-third of controls **(*n*=5,176, 36.0%).** The most commonly prescribed anxiolytic was diazepam which accounted for 81.2% of all anxiolytic prescriptions.

Antidepressant medications were prescribed to over half of cases **(*n*=8,542, 59.2%)** and controls **(*n*=7,858, 54.7%)**. Selective serotonin reuptake inhibitors (SSRIs) were most commonly prescribed, particularly sertraline (37.2%) and citalopram (35.1%).

Association with mortality

There was evidence of a 21% unadjusted increased risk of mortality associated with the use of all antidepressants compared to nonusers (OR=1.21; 95% CI 1.16-1.27) which was reduced after being fully adjusted **[OR=1.08; 95% CI 1.02-1.14 (Figure 3)].**

The use of anxiolytics showed a strong association with mortality compared to nonusers before and after being fully adjusted (OR=1.46; 95% CI 1.39-1.53) **[fully adjusted OR=1.26; 95% CI 1.19-1.33 (Figure 3)].**

Sensitivity analyses

Length of exposure period and the **number of prescriptions issued** had no impact on mortality risk.

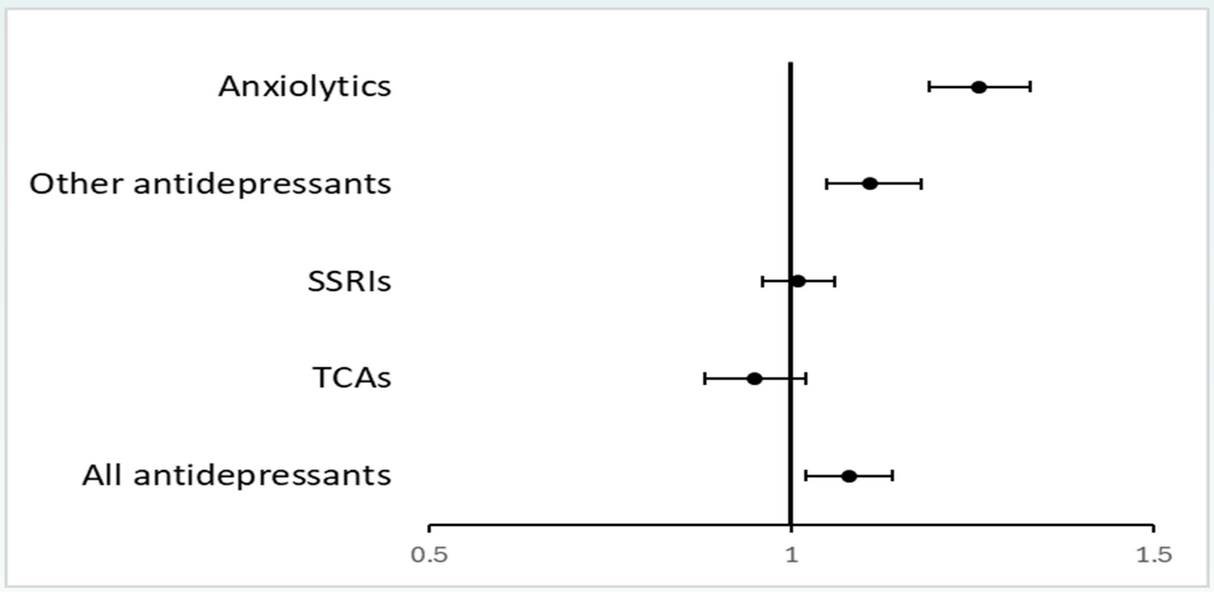

Figure 3: Fully adjusted association between exposure medications and mortality
SSRIs: Selective serotonin reuptake inhibitors; TCAs: Tricyclic antidepressants

Conclusion

In this large population-based study, the use of antidepressants and anxiolytics in PwD was high. The use of antidepressants was associated with a slightly increased risk of mortality whilst the use of anxiolytics was more strongly associated with mortality. Findings from this study contribute to the limited evidence on the prescribing of antidepressant and anxiolytic medications and the associated risk of mortality in PwD.

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